

**Amendments to the Specification:**

*Please amend the paragraph beginning on page 1, line 4 as follows:*

This application is a divisional application of U.S. Application No. 10/358,835, filed February 5, 2003, now allowed, which claims the benefit of priority of U.S. Provisional Application No. 60/354,339 filed February 5, 2002, both of which are hereby incorporated by reference.

*Please amend the paragraph beginning on page 21, line 6 as follows:*

Another embodiment (5) of the invention is a compound according to any one of embodiments (1) to (2) wherein:

X is CH<sub>2</sub>;

R<sup>1</sup> is H;

R<sup>2</sup> is methyl;

R<sup>3</sup> and R<sup>4</sup> are taken together form a 6-membered cyclic ~~morphine~~ morpholine ring.

*Please amend the paragraph beginning on page 21, line 14 as follows:*

Another embodiment (6) of the invention is a compound according to any one of embodiments (1) to (2) wherein:

X is CH<sub>2</sub>;

R<sup>1</sup> is H;

R<sup>2</sup> is ethyl;

R<sup>3</sup> and R<sup>4</sup> are taken together form a 6-membered cyclic ~~morphine~~ morpholine ring.

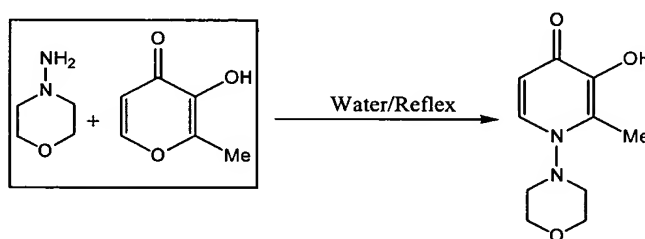
*Please amend the paragraph beginning on page 35, line 12 as follows:*

**Materials.**    ~~4-Aminomorphine~~ 4-Aminomorpholine, 1-aminopiperidine, ammonium chloride, benzoylhydrazine, ethylmaltol, isonicotinic acid hydrazide, maltol, nicotinic acid

hydrazide, phenylsulfonylhydrazide, sodium ascorbate, and thiophenecarboxylhydrazide were purchased from Aldrich, and were used as received.  $^{111}\text{InCl}_3$  (in 0.05 N HCl) were purchased from NEN<sup>®</sup>, N. Billerica, MA.

*Please amend the paragraph beginning on page 36, line 19 as follows:*

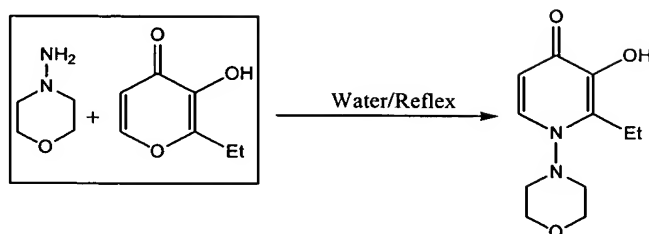
Example II - Synthesis of ~~N-(1-Morphinyl)-2-Methyl-3-Hydroxy-4-Pyridinone~~ N-(1-Morpholinyl)-2-Methyl-3-Hydroxy-4-Pyridinone (MMHP)



Maltol (3.6 g, 30 mmol) and ~~1-aminomorphine~~ 1-aminomorpholine (4.5 g, 45 mmol) were suspended in 100 mL of water. The mixture was heated to reflux for 2 days to give a dark brown solution. The solvent was removed under vacuum to give a black residue. Upon standing at room temperature overnight, a solid was formed. The solid was collected by filtration and was then recrystallized in a mixture of water/methanol (2:1=v:v) to give brownish solid. The product was collected by filtration, washed with cold methanol, and dried under vacuum overnight. The yield was 0.60 g (~9.5%). LC-MS:  $M/z = 211.2$  for  $[\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_3]^+$ .  $^1\text{H}$  NMR (600 MHz, in  $\text{CD}_3\text{OD}$ , chemical shift in ppm relative to TMS): 2.50 (s, 3H,  $\text{CH}_3$ ); 3.00 (d, 2H,  $J_{\text{HH}} = 10.9$  mHz,  ~~$\text{CH}_2/\text{morphine}$~~   $\text{CH}_2/\text{morpholine}$ ); 3.29 (m, 2H,  ~~$\text{CH}_2/\text{morphine}$~~   $\text{CH}_2/\text{morpholine}$ ); 3.79 (m, 2H,  ~~$\text{CH}_2/\text{morphine}$~~   $\text{CH}_2/\text{morpholine}$ ); 4.00 (d, 2H,  ~~$\text{CH}_2/\text{morphine}$~~   $\text{CH}_2/\text{morpholine}$ ); 6.53 (d, 1H,  $J_{\text{HH}} = 7.5$  mHz,  $\text{CH}_2/\text{pyridinone}$ ); and 8.09 (d, 1H,  $J_{\text{HH}} = 7.5$  mHz,  $\text{CH}/\text{pyridinone}$ ).

*Please amend the paragraph beginning on page 37, line 14 as follows:*

Example III - Synthesis of ~~N-(1-Morphinyl)-2-Ethyl-3-Hydroxy-4-Pyridinone~~ N-(1-Morphinyl)-2-Ethyl-3-Hydroxy-4-Pyridinone (MEHP)



To a round-bottom flask were added ethylmaltol (3.2 g, 24 mmol), **1-aminomorphine** **1-aminomorpholine** (4.0 g, 40 mmol) and 100 mL of water. The mixture was heated to reflux for 2 days to give a dark brown solution. Upon removal of the solvent, the dark residue was re-dissolved in a mixture of hot water/methanol (50%:50%=v:v) in the presence of ~~chareol~~ **charcoal**. The mixture was filtered while hot. Solvents were removed under vacuum to give a black residue. After standing at room temperature for 2 days, a solid was formed. The solid was collected by filtration and was then recrystallized in a mixture of water/methanol (2:1=v:v) to give brownish microcrystals. The product was collected by filtration, washed with cold methanol, and dried under vacuum overnight. The yield was 0.48 g (~8.9%). LC-MS:  $M/z = 225.3$  for  $[C_{11}H_{16}N_2O_3]^+$ .  $^1H$  NMR (600 MHz, in  $CD_3OD$ , chemical shift in ppm ~~relative~~ **relative** to TMS): 1.26 (t, 3H,  $CH_3$ ); 2.95 (m, 4H,  $J_{HH} = CH_2/ethyl$  and morphine); 3.33 (m, 2H,  $CH_2/morphine$ ); 3.80 (m, 2H,  $CH_2/morphine$ ); 4.00 (m, 2H,  $CH_2/morphine$ ); 6.49 (d, 1H,  $J_{HH} = 7.5$  mHz, CH/pyridinone); and 8.05 (d, 1H,  $J_{HH} = 7.5$  mHz, CH/pyridinone).